CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

ALKYL (50% C14, 40% C12, 10% C16) DIMETHYL BENZYL AMMONIUM CHLORIDE

Chemical Code # 001846, Tolerance # 50238
SB 950-408

September 4, 1987
Revised: 8/20/90
Revised: 7/29/94, Updated: 6/17/97

I. DATA GAP STATUS

Combined rat: Chronic and onco	No data gap, no adverse effect
Chronic dog:	No data gap, no adverse effect
Onco mouse:	No data gap, no adverse effect
Repro rat:	No data gap, no adverse effect
Terato rat:	No data gap, no adverse effect
Terato rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome:	No data gap, no adverse effect
DNA /Other:	No data gap, no adverse effect
Neurotox:	Not required at this time

Data for this substance and several others (see SUMMARY OF TOXICOLOGY DATA for SB# 408, tolerance # 50238) are grouped for evaluation of possible adverse effects. One-liners for these compounds are compiled in the SUMMARY OF TOXICOLOGY DATA for SB#408, tolerance #50238.

Note, Toxicology one-liners are attached
** indicates acceptable study
Bold face reference number indicates possible adverse effect

File name: T970617
Revised by H. Green & M. Silva, 8/20/90; J. Kishiyama & P. Iyer 6/17/97.

In accordance with California Administrative code Section 6198.5b, data for the following are grouped for evaluation of possible adverse effects. One-liners for these compounds are compiled in the SUMMARY OF TOXICOLOGY DATA for SB#408, tolerance #50238.

SB#408, tolerance# 50238 alkyl (50%C14, 40%C12, 10%C16) dimethyl benzyl ammonium chloride;
SB#138, tolerance# 50354 alkyl (60%C14, 30%C16, 5%C12, 5%C18) dimethyl benzyl ammonium chloride;
SB#409, tolerance# 50352 alkyl (25%C12, 60%C14, 15%C16) dimethyl benzyl ammonium chloride;

SB#410, tolerance# 50698 alkyl (47%C12, 18%C14, 10%C18, 10%C16, 15%C8-C10 dimethyl benzyl ammonium chloride;
SB#411, tolerance# 50699 alkyl (50%C12, 30%C14, 17%C16, 3%C18) dimethyl benzyl ammonium chloride;
SB#161, tolerance# 50353 alkyl (58%C14, 28%C16, 14%C12) dimethyl benzyl ammonium chloride;
SB#419, tolerance# 50700 alkyl (61%C12, 23%C14, 11%C16, 5%C8-C10-C18) dimethyl benzyl ammonium chloride;
SB#412, tolerance# 50701 alkyl (65%C12, 25%C14, 10%C16) dimethyl benzyl ammonium chloride;
SB#413, tolerance# 50424 alkyl (67%C12, 25%C14, 7%C16, 1%C8-C10-C18) dimethyl benzyl ammonium chloride;
SB#414, tolerance# 50413 alkyl (90%C14, 5%C12, 5%C16) dimethyl benzyl ammonium chloride;
SB#415, tolerance# 50702 alkyl (93%C14, 4%C12, 3%C16) dimethyl benzyl ammonium chloride;
SB#840, tolerance# 50831 Roccal-R (61%C12, 23%C14, 11%C16, 5%C18) dimethyl benzyl ammonium chloride;
SB#458, tolerance# 50522 Tetradecyldimethyl benzyl ammonium chloride.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Each individual worksheet may contain additional effects.

COMBINED (CHRONIC/ONCOGENICITY) RAT

Since oncogenic effects were not observed and specific target organs not identified, adverse effects are not indicated in the overall weight of evidence from the several studies (P. Iyer, 4/20/95).

**224 089837, 318 134202, "Chronic Dietary Toxicity/Oncogenicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Rats", (M.W. Gill, S.J. Hermansky, and C.L. Wagner, Bushy Run Research Center, Laboratory ID 53-543, 7/8/91). ADBAC, ai 81.09%, administered in the feed at concentrations of 0, 300, 1000, or 2000 ppm to 60 Sprague-Dawley rats/sex/group for 104 weeks. Body weight was lowered slightly and food intake reduced for the high dose group. No evidence of oncogenicity. NOEL = 1000 ppm in the diet. NOAEL = 1000 ppm in the diet. Initially considered unaccepatable, possibly upgradable upon submission of rational for dose selection. (Kishiyama, and P. Iyer, 2/07/94). ACCEPTABLE (rationale for dose selection from results of range finding studies provided [50238-286 132366 and 50238-319 134225]). P. Iyer, 4/18/95.

318 134202 Rebuttal to 089837

CHRONIC RAT

50238-146 067160 "Toxicology of Benzalkonium Chloride Given Orally in Milk or Water to Rats and Dogs," (Coulston, F., Drobeck, H.P., Mielens and Garvin, Jr., P.J., Section of Experimental Pathology and Toxicology, Sterling-Winthrop Research Institute, Rensselaer, New York. Published in Toxicology and Applied Pharmacology, 3:584-594, 1961. This study compares effects of BAC when administered via stomach tube, rather than by diet, in order to get a more accurate quantification of benzalkonium chloride (BAC) administered.
RATS: BAC was administered by gavage (1 dose/day; prepared fresh daily) to 6 groups of male Sprague-Dawley rats (BW average = 130 g; 10 rats/group) at 0 (vehicle = milk or water), 50 or 100 mg/kg for 12 weeks. NOEL = 50 mg/kg (soft stools after 7 weeks in milk and water groups; 2 deaths in water group after 9 weeks; depressed bodyweight--29% of control throughout treatment with water). **DOGS:** BAC was administered by gavage to 6 groups (3 dogs/group) of beagle dogs (BW

= 6.6 - 9.3 kg--sex unspecified) at 0 (vehicle = water or milk), 12.5, 25 or 50 mg/kg for 52 weeks. NOEL < 12.5 mg/kg (At ≥ 25 mg/kg salivation with both vehicles was observed. All water vehicle dogs died at 25 mg/kg and 1 died at 50 mg/kg--vomiting was observed with treatment. Soft stools were observed in animals treated with both vehicles at 50 mg/kg. BAC in water vehicle caused moderate to severe irritation to the stomach at all doses. At ≥ 25 mg/kg in water, the dogs had moderate to severe irritation and congestion of the stomach and intestines and areas of moderate to severe pulmonary congestion with hemorrhage and pneumonia. Small areas of intestinal hyperemia were observed at ≥ 25 mg/kg, both grossly and histologically with milk vehicle. Congestion and subacute inflammation of the intestine were observed at 12.5 mg/kg and this effect became more severe with dose increase.) No adverse effect was indicated in rats or dogs. **Conclusion:** BAC was tolerated at doses higher than the recommended sanitary use concentrations when data are compared on a calculated dose for dose basis (dietary vs. stomach tube). The study contained no individual data and constitutes supplemental information only. M. Silva, 7/5/90.

50496-003 019908 "Chronic Oral Toxicity Studies on White Rats: Chronic Study Data," (Lab and date not specified). BTC-50 U.S.P. was administered by oral gavage at 0 (vehicle = water), 5, 12.5 and 25 mg/kg/day to "white rats" (12 males and 13 females/group) for 2 years. The diet consisted of dog chow supplemented with ground meat, oranges and vegetable greens. No adverse effects indicated. NOEL = 12.5 mg/kg (A decreased weight gain was observed at 15 months with 25 mg/kg). UNACCEPTABLE (There were many deficiencies but some of the major ones were uncontrolled diet, too few animals/group and no individual animal data). Not upgradeable. (Harnois, 4/13/87).

50238-086 038552 "Toxicology of Benzalkonium Chloride Given Orally in Milk and Water to Rats and Dogs: Rat Chronic," (Winthrop Labs, 5/9/61). Roccal was given in water or milk to Sprague Dawley rats (10 males/group) at concentrations of 0 (vehicle = water), 50 or 100 mg/kg/day for 12 weeks by oral gavage. **Possible adverse effect indicated** (2 deaths and all animals showed a depressed growth rate at 100 mg/kg/day). Apparent NOEL (systemic) = 50 mg/kg/day. UNACCEPTABLE (short time of exposure, too few animals, only one sex tested, no individual animal data, incomplete test description). Not upgradeable. (Harnois, 4/8/87).

50424-002 033664 "Toxicity Studies on Alkyldimethylammonium Chloride in Rats and Dogs: Rat Study," (Michigan State University, East Lansing, MI, in J. Am. Pharm. Assoc. 1951, Vol XL, No 6: p 263-266). Roccal (% a.i. unknown) was used in diet at 0, 0.015, 0.031, 0.062, 0.125, 0.25 and 0.5% and fed to albino rats (Michigan State, 12/sex/group) for 728 days. **Possible adverse effect indicated** (At 0.5%, 50% of the animals were dead by 50 days. Approximately 1/2 of the animals at 0.25% and approximately 1/3 of animals in the control and groups at ≤ 0.125 lived to sacrifice. Acute gastritis was noted in the high dose animals found dead. There was decreased food consumption and weight gain in the survivors.) NOEL (systemic) = 0.25% as given. UNACCEPTABLE (no purity data, no analysis of diet, insufficient numbers of animals, no individual animal data). Not upgradeable. (Harnois, 4/9/87).

Sub-Chronic

50238-286 132366 "Ninety Day Dietary toxicity study with ADBAC in rats." Doses of 0, 100, 500, 1000, 4000 or 8000 ppm, 15/sex/group. No worksheet. (Iyer, 4/21/95).

50238-319-134225 "Two week dose range finding screen with ADBAC in rats." No worksheet.

DOG

278 130007, 318 134207, "Evaluation of ADBAC in a One-Year Chronic Dietary Toxicity Study in Dogs", (Edwin I. Goldenthal, International Research and Development Corporation, MI., Report # 638-004, 3 May 1994). The test article is identified as commercial grade 80% manufacturing use product alkyl dimethyl benzyl ammonium chloride with alkyl chain length distribution of 40%C12, 50%C14, and 10%C16 and 81.09% purity. Four dogs/sex/group received concentrations of 0, 120, 400, and 1200 ppm in the diet for 1 year. Slight bodyweight reduction (3.5% to 8%) was noted for both sexes at 1200 ppm. All dogs in all groups, had mineralization of the kidneys. Two neoplastic findings were noted: one mid-dose male with a benign melanoma of the eyelid and one low-dose female with histiocytoma of oral tissues. **Adverse effects are not indicated. NOAEL = 1200 ppm. Chronic NOEL = 400 ppm (reduced food consumption and decreased cholesterol values were recorded for both sexes at 1200 ppm). Initially considered as **unacceptable**, upgradeable with test article grade clarification and range-finding data. (H. Green and P. Iyer 7/28/94). Upgraded with clarification of test article grade and submission of range-finding data [50238-320 134226, 50238-321 134227 and 50238-322 134228]. Acceptable (P. Iyer 4/19/95).

50238-146 067160 See "Chronic Rat," above (same record #).

50238-086 012307 "Toxicology of Benzalkonium Chloride Given Orally in Milk and Water to Rats and Dogs: Dog Chronic," (Winthrop Labs, 5/9/61). Roccal 0, 12.5, 25 or 50 mg/ml/day in water or milk was given to beagle dogs (3/group) for 52 weeks (?6 days/week) by oral gavage. NOEL = 12.5 mg/ml/day (Dogs treated with water-vehicle preparation died by day 197 at 25 mg/ml/day but 2/3 in the 50 mg/ml/day group survived to sacrifice after displaying symptoms of vomiting, soft stool and excess salivation). The initial review (Aldous, 6/4/85) stated that there was insufficient information for assessment. A subsequent review noted adverse effects (gastric symptoms). UNACCEPTABLE (test article not characterized; dog history was not clear; too few animals/group; no individual data; amount of Roccal absorbed was questionable due to GI symptoms). Not upgradeable. (Harnois, 9/11/87).

50424-002 033664 "Toxicity Studies on Alkyldimethylammonium Chloride in Rats and Dogs," (Michigan State University, East Lansing, MI, in J. Am. Pharm. Assoc., 6/51). Roccal (% a.i. was not stated) was fed in diet to mongrel dogs (no sex specified) for 15 weeks at 0.031, 0.062, 0.125, 0.25 and 0.5% (1 dog/group) and 1% (2 dogs). No control group was used. **Possible adverse effect indicated**. NOEL (systemic) = 0.125% (At $\geq$ 0.25% Roccal there was a decrease in body weight and to a lesser degree, food consumption was also reduced. There was 1 death each at 0.5 and 1%. Erosion of the stomach and small intestine was visible at $\geq$ 0.5%). NOAEL = 0.25% Roccal. UNACCEPTABLE (No purity information or diet analysis were provided. There were insufficient numbers of animals in the study. The dogs were not described nor was their breed defined. There were no individual animal data.) Not upgradeable. (Harnois, 4/9/87).

Sub-Chronic

320 134226, "Evaluation of ADBAC in a two-week palatability study in dogs." No worksheet (Iyer, 4/19/95).

321 134227, "Evaluation of ADBAC in a two-week gavage study in dogs." No worksheet (Iyer, 4/19/95).

322 134228, "Evaluation of an eight-week dietary toxicity study in dogs." No worksheet (4/19/95).

ONCOGENICITY RAT

See Combined (chronic/oncogenicity) rat

MOUSE

** 216 096692, "Chronic Dietary Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Mice", (M.W. Gill, S.J. Hermansky and C.L. Wagner, Bushy Run Research Center, Laboratory Project ID 53-515, 1/9/91). ADBAC, purity 81.09%, incorporated in the feed at concentrations of 0, 100, 500, or 1500 ppm to 60 CD*-1 mice/sex/group for 18 months. Body weights were lower throughout the study for high dose groups. High dose males and females lost body weight during the initial week of dosing before showing any weight gains. Initially, body weight gains were depressed approximately 88% and stabilized to approximately 15% to 27% during most of the remaining study. No evidence of oncogenicity. NOEL = 500 ppm based on reduced body weight and body weight gain. ACCEPTABLE. (Kishiyama and P. Iyer, 11/05/93).

REPRODUCTION RAT

217 096687, 318 134209, "Two-Generation Reproduction Study in Sprague-Dawley (CD*) Rats with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered in the Diet", (T. L. Neeper-Bradley, Bushy Run Research Center, Laboratory Project ID 52-524, 1/30/90). ADBAC (purity 81.09%), in the feed at 0, 300, 1000, 2000 ppm through two generations (1 litter per generation) of 28 Sprague-Dawley rats/sex/group/generation. The effects of ADBAC was limited to reduced food consumption and body weight values that were statistically significant and occurred mostly during the pre-breeding period for the F0 and F1 high dose group, and during gestation for F1 females at the high dose. Body weight was also lower for F1 & F2 pups at late lactation and weaning. The reduced food consumption and bodyweight may be a result of unpalatability of the feed/test article mixture at the high dose. NOEL = 1000 ppm (maternal); > 2000 ppm (reproduction). Initially considered as **unacceptable, upgradable upon submission of rationale for dose selection (Kishiyama, and P. Iyer, 11/29/93).
Acceptable (rationale for dose selection provided by submission of range finding [50238-319 134225] and sub-chronic studies [50238-286 132366]) P. Iyer, 4/20/95.

50496-003 019908 "Chronic Oral Toxicity Studies on White Rats: Reproduction Data," (Lab and date not specified). BTC-50 U.S.P. was administered by oral gavage at 0 (vehicle = water), 5, 12.5 and 25 mg/kg/day to "white rats" (12 males and 13 females/group) for 2 years. The diet consisted of dog chow supplemented with ground meat, oranges and vegetable greens. No adverse effects indicated. Parental NOEL = 12.5 mg/kg (A decreased weight gain was observed at 15 months with 25 mg/kg). Reproduction NOEL $\geq$ 25 mg/kg/day (No reproductive effects were observed from the data presented). Pup NOEL cannot be evaluated since no F1 or F2 data were provided. UNACCEPTABLE (There were many deficiencies but some of the major ones were uncontrolled diet, too few animals/group, too few litters and no individual animal data). Not upgradeable. (Harnois, 4/13/87).

TERATOLOGY

** 238 115356, "Developmental Toxicity Evaluation II of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to CD* Rats", (T.L. Neeper-Bradley, Bushy Run Research Center (BRRC), Laboratory Project ID 91N0031, 6/8/92). ADBAC, purity 81.09%, was administered at concentrations of 0 (Milli*-Q water), 10, 30, or 100 mg/kg/day during days 6 through 15 of gestation to 25 pregnant CD* rats/group. Perioral wetness was observed in 17 (3 with audible respiration) high-dose dams and 1 mid-dose dam (with audible respiration); also, another mid-dose dam without perioral wetness exhibited audible respiration; Maternal NOEL = 10 mg/kg/day. No fetal abnormalities were evident; Developmental NOEL >100 mg/kg/day. ACCEPTABLE. (Kishiyama, and P. Iyer, 11/12/93).

253 121051, "Developmental Toxicity Dose Range-Finding Study of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to CD* Rats", (J.S. Chun and L.C. Fisher, Bushy Run Research Center (BRRC), Laboratory ID 54-613, 1/20/93). Alkyl dimethyl benzyl ammonium chloride (ADBAC, 81.09% purity), administered by oral gavage at concentrations of 0 (Milli-Q* water), 25, 50, 100, 200 or 400 mg/kg/day to 5 CD* [Crl:CD* BR] rats/group on days 6 through 15 of gestation. Animals in the 200 and 400 mg/kg groups died before scheduled sacrifice. Perioral wetness and audible respiration were observed for the 100 mg/kg/day group. Due to concern for maternal death in the main study, 100 mg/kg is suggested as the maximum dose that may limit mortality and yet produce maternal toxicity. This study is limited by the small number of animals/group and lacks visceral and skeletal examination of fetuses. Supplemental (Kishiyama, and P. Iyer, 11/15/93).

50238-125 051397 "Teratologic evaluation of BTC-8358 in rats" (FDRL, 8-30-77) BTC-8358 was administered to BLU(SD)BR rats (at least 20/group) by oral gavage at 5, 15, 50 mg/kg in water on days 6-15 of gestation (day 0 = vaginal plug +) at 10 ml/kg. Controls (aspirin and water) common to study in CDFA #50354-176 19907. **Adverse effects** (higher number of fetuses with rudimentary ribs at 50 mg/kg). Maternal NOEL $\geq$ 50 mg/kg/day (HTD); Presumptive developmental NOEL = 15 mg/kg (rudimentary ribs). NOT ACCEPTABLE (no individual data given for clinical signs, food consumption by dams, or fetal examinations; no historical control data given; no justification given for maximum dose). Not upgradeable. (Harnois, 3/27/87).

50238-136 019895 Exact duplicate of 051397.

50238-132 067118, "Teratologic Evaluation of Four Quaternary Compounds (Barquat MB-50; Barquat MX-50; Barquat 4250; Barquat 4250-Z)", (Knickerbocker, M. and Stevens, K.R., Food and Drug Research Laboratories, Inc., Laboratory # 5154, 2/11/77). Barquat MB-50 (lot # B3730; 50% n-alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chloride; 10% ethanol, 40% inerts), Barquat MX-50 (lot # B3407; 50% n-alkyl (60% C14, 30% C12, 5% C16, 5% C18) dimethyl benzyl ammonium chloride; 10% ethanol, 40% inerts), Barquat 4250 (lot # B3308; 25% n-alkyl dimethyl benzyl ammonium chlorides, 25% n-alkyl dimethyl ethylbenzyl ammonium chlorides, 50% inerts) and Barquat 4250-Z (lot # B3668; 25% n-alkyl dimethyl benzyl ammonium chlorides, 25% n-alkyl dimethyl ethylbenzyl ammonium chlorides, 50% inerts) were administered by gavage on days 6 through 15 of gestation (detection of sperm plug = day 0 of gestation) to 22 - 51 mated FDRL/Wistar derived female rats/dose/chemical group at 0 (water), 10, 25, or 50 mg/kg/day. No maternal or fetal effects were observed. No adverse effects indicated. NOEL maternal and fetal $\geq$ 50 mg/kg/day. UNACCEPTABLE (An MTD was not obtained, therefore the adequacy of the high dose was not demonstrated. The report consists of summary information only, there were no individual data. The age of the animals used in the study and the process used for assignment to treatment groups was not mentioned. A QA was not provided.) The study may be upgradeable. (H. Green & M. Silva, 6/25/90).

50238-230 112034, Supplement to 50238-132 #067118 "Teratologic Evaluation of Four Quaternary Compounds (Barquat MB-50; Barquat MX-50; Barquat 4250; Barquat 4250-Z)", (Knickerbocker, M. and Stevens, K.R., Food and Drug Research Laboratories, Inc., Laboratory # 5154, 12/19/91). The supplemental data did not include an MTD and therefore the adequacy of the high dose was not demonstrated; dose justification lacks reference support. **Unacceptable** Possibly upgradable with submission of data demonstrating that 100 mg/kg/day is a MTD (P. Iyer, 11/10/93).

50354-158, 176 019904, 019906, 019907 "Teratologic Evaluation of BTC-E-2125M (80% active) in Rats," (Food and Drug Research Laboratories, Waverly, NY, 9/77, #5433A). BTC-E-2125M, in water, was administered at concentrations of 0, 5, 15 and 50 mg/kg/day by oral gavage to mated BLU: (SD) rats ($\geq$ 20/group on days 6-15 of gestation where day 0 = vaginal plug detectable). Controls (aspirin and water) were also used in study 051397. Maternal NOEL $\geq$ 50 mg/kg (HTD). **Possible adverse effect indicated.** Presumptive Developmental NOEL = 15 mg/kg (An increase in the number of fetuses with rudimentary ribs at 50 mg/kg/day was observed.) NOT ACCEPTABLE (test material was not characterized; no justification of maximum dose, there was inconsistency in the number of animals reported, no analysis of dosing solution, no maternal clinical observations and a limited statistical treatment of data was presented).

(Schreider, 6/4/85).

50353-060 035967 "Teratology Study in Rats--BioQuat 50-38. Final Report," (Warf Institute, Inc., Madison, WI. Report #: 6091680, 5/77). BioQuat 50-28 was administered by gavage to mated CD female rats (20/group for necropsy, 10/group for natural delivery) at 0 (vehicle = water), 4, 20 and 95 mg/kg/day on days 5-14 of gestation (day 0 of gestation = day of mating). Maternal NOEL = 20 mg/kg/day (7/30 animals died, and there was abdominal distention with little or no food present as well as decreased body weight gain was observed at 95 mg/kg/day). Fetal NOEL = 95 mg/kg/day (Increased resorptions and decreased fetal weight was observed at 95 mg/kg/day. No remarkable findings were observed in naturally delivered pups.) No adverse effects indicated. Initially reviewed by Apostolou (11/6/85) as unacceptable but possibly upgradeable (Dosing material was not analyzed and body weights used to calculate dosage were not specified. Maternal clinical observations and necropsy data were incomplete. No historical control data were provided for fetal abnormalities and there were no individual data for delivered pups.) A subsequent review noted an apparent maternal NOEL = 20 mg/kg/day and an apparent developmental NOEL $\geq$ 95 mg/kg/day. Not upgradeable due to too much missing data. (Harnois, 9/10/87).

Summarizing the rat teratology studies, no fetal abnormalities were evident indicating that the developmental NOEL >100 mg/kg/day and the maternal NOEL = 10 mg/kg/day (perioral wetness/ audible respiration). (Iyer, 2/11/94).

**244 116248, 318 134211, "Developmental Toxicity Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to New Zealand White Rabbits", (G. P. Schoenig, PhD. Toxicology Consultant to the ADBAC Quat Joint Venture/ Chemical Specialties Manufacturers Association, 2/14/96). ADBAC, purity 81.09%, was administered at concentrations of 0 (water), 1.0, 3.0 or 9.0 mg/kg/day during days 6 through 18 of gestation to 16 pregnant New Zealand White rabbits per group. In the high dose group, one rabbit was hypoactive with labored breathing and another demonstrated audible respiration, symptoms characteristic of ADBAC toxicity. There was a slight increase in fetal malformation (dilated lateral ventricle) and variation (poor skeletal ossification) in the mid and high dose groups. Maternal NOEL = 3 mg/kg/day; Developmental NOEL = 1 mg/kg/day. Initially reviewed as unacceptable, upgradable with historical control data for the incidence of lateral ventricle dilatation (J. Kishiyama and P. Iyer, 11/16/93). Acceptable (adequacy of high dose justified [#134211]). Possibility of adverse effect (P. Iyer, 4/20/95) clarified upon submission of some of the requested information regarding historical control data. The study is reviewed to be acceptable without being flagged as a possible adverse effect (P. Iyer, 6/12/97). No Record #, filed under SBR- 159546-E as W 116248.s02.

50238 257 122620, "Developmental Toxicity Dose Range-Finding Study of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to New Zealand White Rabbits", (J.S. Chun and T.L. Neeper-Bradley, Bushy Run Research Center (BRRC), Laboratory Project ID 54-603, 3/9/93; conducted June-July 91). ADBAC, purity 81.09%, was administered at concentrations of 1.0, 3.0, 10.0 30.0, or 60 mg/kg/day during days 6 through 18 of gestation to 5 pregnant New Zealand White rabbits/group. Exposure resulted in mortality (100% at 60 mg/kg and 40 % at 30 mg/kg) in the two high dose groups. At the 10 mg/kg group body weight loss, reduced food consumption and signs of clinical toxicity were observed. Treatment-related embryotoxicity or developmental toxicity including teratogenicity was not observed in any dose group. On the basis of this study, target doses selected for the definitive rabbit teratology study were 0, 1.0, 3.0 and 9.0 mg/kg/day (Iyer, 11/16/93).
No worksheet.

50238-132 067158, "Teratogenic Evaluation in Rabbits, Hyamine 3500, Final Report", (No author was named, Hazleton Laboratories America, Inc., project # 417-364, 1/6/78). Hyamine 3500 (no purity or lot # was provided) was administered by gavage to 15 female rabbits/group on gestation days 7 through 19 at 0 (distilled water), 10, 30, and 100 mg/kg/day. It was not stated whether the animals were artificially inseminated or mated. NOEL maternal < 10 mg/kg/day: At 100 mg/kg, anorexia, nasal discharge,

depression, thinness and/or cyanosis was observed and 15/15 died by day 12. "Gross pathology" was observed in trachea, lungs, gallbladder, liver, stomach and/or kidneys in all but one doe at 100 mg/kg and 9/15 were pregnant. 3/15 (2/15 by day 19) and 6/15 (4/15 by day 19) died at 10 and 30 mg/kg/day respectively. The same clinical signs were observed at 10 and 30 mg/kg as were seen at 100 mg/kg. Gross alterations of trachea, lungs, gallbladder, liver, stomach and/or kidneys were observed in animals that died at 30 mg/kg. Livers with friable consistency were noted in mid-dose animals sacrificed on day 29. Fetal NOEL < 10 mg/kg/day: At $\geq$ 10 mg/kg, signs of embryotoxicity (fetal death) was observed and considered treatment-related (probably due to toxic effects in the dam). No fetuses were available at 100 mg/kg for evaluation. No adverse fetal effects indicated, however, it appears that the mid and high doses may have been too high. The maternal necropsy revealed a frequent incidence of gross alterations of the trachea, lungs, gallbladder, liver (friable consistency), stomach and/or kidneys at 30 mg/kg/day. Hyamine 3500 does not appear to be teratogenic at the doses tested. UNACCEPTABLE (summary data only, not a full study.) (H. Green & M. Silva, 6/26/90).

GENE MUTATION

** 50238-146 087573, "Mutagenicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the CHO/HGPRT Forward Mutation Assay", (Young, R.R., Hazleton Laboratories America, Inc., Kensington, Maryland, study # 10238-0-435, 1/23/89). N-alkyl dimethyl benzyl ammonium chloride (ADBAC QUAT, 80% composite; manufacturing use product; LOT # 7293K) was used in a forward mutation assay (4 hour treatment) on CHO-K1-BH_4 Chinese Hamster ovary cells with S9 from Aroclor 1254 (500 mg/kg) induced male Sprague Dawley rat livers at 0 (sterile deionized water), 1, 5, 10, 20, 22, 24, 26, 28, 30, 40, 50, 65, 85, and 100 mg/ml and without S9 at 0 (sterile deionized water), 1, 5, 10, 12, 13, 14, 16, 18, 20, 24, 25, 35, 50, and 65 mg/ml. All dose levels were not replicated. No significant increases in mutant frequencies either with or without S9 were observed when compared with the positive control. ACCEPTABLE. No adverse effect. (H. Green & M. Silva, 6/22/90)

CHROMOSOME

** 50238-132 067159, "Assessment of the mutagenic activity of Hyamine 3500 in the Mouse Micronucleus Test", (T. Kallesen, Scantox Laboratories Ltd., laboratory # 10753, 12/16/85). Hyamine 3500 (80.2% pure; Lot #: L5383) was administered as a single dose by gavage at 400 mg/kg to 15 Bom:NMRI mice/sex. 5/sex were sacrificed at 24, 48, and 72 hours post-treatment. 5/sex were treated with cyclophosphamide at 30 mg/kg (24 hour sacrifice) as a positive control and distilled water served as a negative control. A reduced polychromatic erythrocyte count was observed at 24, 48, and 72 hours in Hyamine 3500 treated groups, however no effect on micronuclei formation was observed. ACCEPTABLE. (H. Green & M. Silva, 6/26/90).

DNA /OTHER GENETIC

** 50238-146 087574, "Mutagenicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay", (Cifone, M.A., Hazleton Laboratories America, Inc., Kensington, MD., Study # 10238-0-447, 2/16/89). Alkyl dimethyl benzyl ammonium chloride (ADBAC QUAT 80% Manufacturing use product; code # 349006; lot #: 7293K; clear, pale liquid) was used in an unscheduled DNA synthesis assay with male Fischer 344 rat primary hepatocytes (3 plates/dose; 50 cells scored/plate) at 0 (sterile deionized water), 0.319, 0.531, 1.060, 3.190, 5.310, and 6.370 mg/ml. 2-AAF at 0.1 mg/ml (3 plates/dose) served as a positive control. No significant increase in unscheduled DNA synthesis was observed. Positive controls functioned as expected. ACCEPTABLE. (H. Green & M. Silva, 6/25/90)

ADDITIONAL USEFUL SUMMARY DATA

The following documents contain summary data for several substances.

50238-086 012302 (038551 is draft; includes 011155) "Quaternaries as swimming pool algicides" (Quaternary Subcommittee of Chemical Specialties summary document) Description of use of substance and general discussion on absence of toxic effects. No data for review. (Harnois, 4/27/87; filed under SB#408)

50354-255 046252, 046253, 046254, 046255 "Quaternary ammonium surfactants: acute and chronic toxicity" (Association of Food and Drug Officials, Quarterly Bulletin, 4/54). Includes tablular summary of results from several studies. (Harnois, 4/23/87; filed under SB#138)

50354-255 046256-046259 "Toxicology of cationic surfactants" (R.A. Cutler, H.P. Drobeck, Sterling-Winthrop Research Institute. Review chapter in unnamed source). Reviews of most of the studies already on file at CDFA. Also a quick guide to structure, chemical nature and over-all effects. (Harnois, 4/23/87; filed under SB#138).